REMARKS

Claims 1-8 and 10-22 are pending in the present application.

Applicants wish to thank Examiner Raghu for the indication that Claims 2-5, 12-13, and 15-18 are free from the art of record and allowable. Applicants request reconsideration of the outstanding rejections.

The rejections of: (a) Claims 1, 6-8, 10-11, 14, and 19-22 under 35 U.S.C. §112, first paragraph (written description), and (b) Claims 1, 6-8, 10-11, 14, and 19-22 under 35 U.S.C. §112, first paragraph (enablement), are respectfully traversed.

In the outstanding Office Action the Examiner has two criticisms upon which the claims have been rejected as lacking sufficient written description and enablement. The first is the scope of homologs defined by "at least 95% homology" to SEQ ID NO: 2. And, the second is the scope of mutations permitted in the region of positions 343-377 of SEQ ID NO: 2. However, throughout the Examiner's rejections, these two points appear to be randomly interspersed and sometimes confused.

First, with respect to the scope of homology defined as "at least 95%" the Examiner indicates that the precedent of the U.S. PTO's Board of Patent Appeals and Interferences (*Ex parte Bandman*) and the written description guidelines do not apply to all applications. Specifically, the Examiner maintains that the range of homologs permitted by a range of homologs of at least 95% is insufficiently supported by the specification allegedly as a result of the disclosure on pages 8-9 of the specification that the "Three-dimensional structural analysis through homology modeling (Ozawa *et al.*, *Protein Eng.*, *14*, 501-504, 2001) suggests that the amino acid region at the 343rd to 377th positions of SEQ ID NO: 1 is

located relatively distant from the active center of Egl-237 and therefore has a high degree of freedom, and is suggested to be a region that forms a portion of the loop structure that is intimately involved in maintaining the cellulase structure." This is an instance where the Examiner confuses the two issues.

The Examiner is reminded that the scope defined as "at least 95% homology" to SEQ ID NO: 2 refers to the sequence to be modified (i.e., the protein sequence prior to modification of the positions corresponding to positions 343-377 of SEQ ID NO: 2), not the resultant product. Thus, the first question that the artisan should ask is whether the specification as filed allow persons of ordinary skill in the art to recognize that Applicants have invented what is claimed (MPEP § 2163.02). In other words, would the artisan recognize based on the disclosure of the specification that Applicants were in possession of the necessary common attributes possessed by the members of the genus (i.e., the structure and activity of the unmodified protein).

With the foregoing properly in mind, Applicants submit that *Ex parte Bandman* and the written description guidelines are directly germane to the claimed invention and, even under the facts of this application, are properly applied. With respect to the sufficiency of the disclosure for describing the claimed sequence, the Examiner's attention is again directed to Example 14 of the Synopsis of Application of Written Description Guidelines which analyzes a situation where a claim covers a protein that is at least 95% identical to a disclosed sequence and has a specific function. In these guidelines, the Patent Office has concluded that such a claim is adequately described within the meaning of 35 U.S.C. § 112, first paragraph

> There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the

> specified catalytic activity and must have at least *95%* identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least *95%* structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least *95%* identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.
>
> **Conclusion:** The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

As the specification adequately describes the sequences that are at least 95% homologous to SEQ ID NO: 2 (page 5, lines 9-16), the specifically defined mutations within the scope of the claims, and the specification describes how one can test for alkaline cellulase activity as well as how the skilled artisan can prepare, clone, and express mutated alkaline cellulases within the scope of the claimed invention, the claims as presented herein are deemed to be fully described and enabled to the extent that the claims read on the scope of homologs to SEQ ID NO: 2 defined by scope of "at least 95% homology".

Accordingly, the specification adequately meets the current standard of the Office and Applicants should be entitled to the claimed mutated alkaline cellulases. Applicants also submit that the decision by the U.S. PTO's Board of Patent Appeals and Interferences (*Ex parte Bandman*) in which the Board held that claims to amino acid sequences that are at least 95% homologous to the disclosed sequence are adequately described and enabled when the specification describes the nucleotide and amino acid sequences. This decision is consistent with Example 14 of the Synopsis of Application of Written Description Guidelines and the facts of this case. As such, *Ex parte Bandman* also applies to the case at hand and supports the fact that the specification fully describes and enables the full scope of homologs defined by "at least 95% homology" to SEQ ID NO: 2 and having alkaline cellulase activity.

With respect to the Examiner's apparent second ground of criticism, Applicants submit that the scope of mutations permitted in the region of positions 343-377 of SEQ ID NO: 2 only includes those that retain alkaline cellulase activity. Contrary to the Examiner's allegations that a representative number of such modifications are not described and supported by the present specification, the Examiner's attention is directed to the description provided at page 10, line 1 to page 11, line 3. This section describes several peptides to be inserted in addition to those specifically exemplified in the present application. These peptides include not only specifically defined tripeptides, but also specifically defined tetrapeptides, pentapeptides, and hexapeptides.

Further, the Examiner is reminded that the range of possible alterations is not overbroad and poorly defined, but rather is succinct and clear to place the skilled artisan in possession of the full scope of the present invention. In particular, the skilled artisan would appreciate that the claims specifically identify the loop region to be modified as being the 35 amino acid region of positions 343-377 of SEQ ID NO: 2, or the positions corresponding thereto in a protein have at least 95% homology to SEQ ID NO: 2. Further, at page 5, lines 14-16 and page 6, lines 4-7, Applicants provide the skilled artisan two methods by which the level of global homology of the candidate protein may be assessed, as well as how regions corresponding to positions 343-377 of SEQ ID NO: 2 can be identified. Further, to cross-correlate and verify the structural homology of a positive from the sequence homology comparison Applicants disclose several homology modeling methods at page 5, lines 17-21, as well as the characteristics shared thereby (see page 5, line 21 to page 6, line 4.

And, if this were not enough on its own, the claims require that the resulting protein have alkaline cellulase activity. Therefore, proteins lacking this activity are eliminated from consideration regardless of the number of candidate sequences this may embrace.

Accordingly, based on the disclosure of the present specification, the skilled artisan would immediate appreciate the full scope of homologs having at least 95% homology to SEQ ID NO: 2 and would be able to readily appreciate the region corresponding to positions 343-377 of SEQ ID NO: 2. At this point is it a routine, almost mechanical act, to select the residue(s) to delete and the desired peptides to insert, all of which would be clearly appreciated from the description in the present specification. Upon establishing the scope of candidate mutated proteins, the skilled artisan need only assess whether the candidate mutated protein still possesses alkaline cellulase activity. To this end, the assay for determining the same is known in the art (i.e., the 3,5-dinitrosalicylic acid method) and is fully described at page 17, line 1 to page 18, line 1. As such, identification of candidate mutated proteins possessing alkaline cellulase activity can be easily and routinely determined.

Granted, the amount of experimentation to be done may be extensive. However, the Examiner should not confuse "quantity of experimentation" with "undue experimentation". In fact, MPEP §2164.06 states:

> ... quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'

Applicants submit that, for the reasons set forth above and with the present specification in hand, determination of sequences that fall within the scope of the claimed invnetion would require nothing more than routine experimentation to determine sequence

homology, mutagenesis (for further guidance to this end the artisan need only refer to the details provided in the Examples on pages 13-19), and protein activity.

Therefore, the claims of the present specification are described and enabled within the context of 35 U.S.C. §112, first paragraph.

Withdrawal of these grounds of rejection is requested.

The objection to Claims 1 and 8 and Claims 6-7 and 19-20 is obviated by amendment. Applicants have amended the claims in accordance with the Examiner's suggestions. Withdrawal of this ground of objection is requested.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

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